

U.S.S.N. 09/978,333

Filed: October 15, 2001

**RESPONSE TO RESTRICTION REQUIREMENT****AMENDMENT**

1-6. (canceled)

7. (currently amended) A method for targeted recombination of a nucleic acid molecule comprising the steps of:

- a) hybridizing providing a single stranded oligonucleotide having a sequence that forms a triple stranded nucleic acid molecule that hybridizes with a target sequence double stranded nucleic acid molecule and a  $K_d$  of less than  $2 \times 10^{-6}$ ; and
- b) recombining providing a donor nucleic acid which recombines into the target sequence, induced by triple helix formation between the single stranded oligonucleotide and double stranded nucleic acid molecule.

8. (original) The method of claim 7, wherein the single stranded oligonucleotide is between 10 and 60 nucleotides in length.

9. (original) The method of claim 7, wherein the single stranded oligonucleotide is tethered to the donor DNA fragment.

10. (original) The method of claim 7 wherein the double stranded nucleic acid molecule encodes a protein and the targeted recombination alters the activity of the protein encoded by the double-stranded nucleic acid molecule.

11. (original) The method of claim 7, wherein the double-stranded nucleic acid molecule is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.

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12. (original) The method of claim 7, wherein the donor fragment is at least 30 nucleotide residues in length.

13-14. (canceled)

15. (currently amended) A The method of claim 7 to produce heritable changes in the genome of an intact human or animal further comprising the steps of:

- a) injecting an oligonucleotide having a sequence that forms a triple stranded nucleic acid molecule with a target region of the genome, and having a Kd of less than  $2 \times 10^{-6}$ , wherein
- b) binding the oligonucleotide binds to the target region, and c) mutating mutates the target region.

16. (original) The method of claim 15 wherein the oligonucleotide is between 10 and 60 nucleotides in length.

17. (original) The method of claim 15 wherein the oligonucleotide is dissolved in a physiologically acceptable carrier.

18. (original) The method of claim 15 wherein the oligonucleotide is recombinogenic.

19. (original) The method of claim 18 wherein the oligonucleotide stimulates recombination of an exogenously supplied DNA fragment with the target region of the genome.

20. (original) The method of claim 18 wherein the oligonucleotide stimulates recombination of a tethered DNA fragment with the target region of the genome.

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21. (original) The method of claim 15 wherein the target region is selected from the group consisting of a gene, an oncogene, a defective gene, a viral genome, and a portion of a viral genome.
22. (original) The method of claim 21 wherein the gene is a defective  $\beta$ -hemoglobin gene, cystic fibrosis gene, xeroderma pigmentosum gene, nucleotide excision repair pathway gene or hemophilia gene.
23. (original) The method of claim 15 wherein the oligonucleotide is composed of homopurine or homopyrimidine nucleotides.
24. (currently amended) The method of claim 15 wherein the oligonucleotide is composed of polypurine or polyrimidine polypyrimidine nucleotides.
25. (original) The method of claim 9 wherein the donor fragment is between 10 and 40 nucleotides.